Applicant: Carol Brugnara et al.

Attorney's Docket No.: 13691-002005 / 470-104US2

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AMENDMENT

Please amend the above-captioned application as follows:

In The Claims:

Please amend claims 1, 3, 4, 6, 7, and 11 as follows:

-- 1. A compound having the structural formula:

$$(I)$$

$$(R_{6})_{n}$$

$$(R_{5})_{n}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

m is 0, 1, 2, 3 or 4;

each n is independently 0, 1, 2, 3, 4 or 5;

X is C;

Y is absent, (C_1-C_6) alkyl, (C_1-C_6) alkenyl or (C_1-C_6) alkynyl;

 R_1 is absent, -OR, -SR, =O, =S, =N-OR, -O-C(O)R, -S-C(O)R, -O-C(S)R, -S-C(S)R, or when taken together with R_2 is a 3-8 membered heterocycloalkyl or a substituted 3-8 membered heterocycloalkyl;

R₂ is absent or -H;

R, is absent or -H;

R₄ is -H, -OR', -SR', -NR'₂, \uparrow CN, -NO₂, (C₃-C₈) cycloalkyl, 3-8 membered heterocycloalkyl, -C(0)R', -C(S)R', -C(0)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'₂ or -C(S)NR'₂;

each R₃, R₆ and R₇ is independently selected from the group consisting of -halogen, -R', -OR', -SR', -NR'₂, -ONR'₂, -SNR'₂, -NO₂, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(O)SR', -C(S)OR', -CS(S)R', -C(O)NR'₂, -C(O)NR'(OR'), -C(S)NR'(OR'); -C(O)NR'(SR'), -C(S)NR'(SR'), -CH(CN)₂, -CH[C(O)R']₂, -CH[C(S)R']₂, -CH[C(S)OR']₂, -CH[C

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each R is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, (C_5-C_{20}) aryl, substituted (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl and substituted (C_6-C_{26}) alkaryl;

the heterocycloalkyl substituents are each independently selected from the group consisting of -CN, -NO $_2$, -NR' $_2$, -OR', $-C(0)NR'_2$, $-C(5)NR'_2$, -C(0)OR', -C(5)OR', -C(0)SR', -C(5)SR'and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of halogen, -C(0)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(O)NR'2, -C(S)NR'2 and trihalomethyl;

each R' is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl and (C_1-C_6) alkynyl;

--- designates a single or double bond; and wherein when X is C and R_1 is =0 or =0H, at least one of R_s , R_s or R_7 is other than -H, or Y is present or R_s is other than -Ha

A pharmaceutical composition comprising a compound and a pharmaceutically acceptable excipient, carrier or diluent, said compound having the structural formula:

(R₅)₀

 $(R_6)_n$

(I)

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or a pharmaceutically acceptable salt or hydrates thereof,
  wherein:
       m is 0, 1, 2, 3 or 4;
       each n is independently 0, 1, 2, 3, 4 or 5;
       X is C;
       Y is absent, (C_1-C_6) alkyl, (C_1-C_6) alkenyl or (C_1-C_6)
 alkyny1;
       R_1 is absent, \sqrt{\frac{1}{1}}OR, -SR, =0, =S, =N-OR, -O-C(O)R, -S-C(O)R,
 -O-C(S)R, -S-C(S)R\ or when taken together with R<sub>2</sub> is a 3-8
 membered heterocycloalkyl or a substituted 3-8 membered
 heterocycloalkyl;
      R, is absent or -H;
      R, is absent or -H;
      R_4 is -H, -OR', -SR', -NR'<sub>2</sub>, -CN, -NO<sub>2</sub>, (C_3-C_8) cycloalkyl,
 3-8 membered heterocycloalkyl, -C(0)R', -C(5)R', -C(0)OR',
 -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR', or -C(S)NR',;
      each Rs, Rs and R, is independently selected from the
 group consisting of -halogen, -R', -OR', -SR', -NR'2, -ONR'2,
 -SNR'_{2}, -NO_{2}, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(O)SR',
-C(S)OR', -CS(S)R', -C(O)NR'_{2}, C(S)NR'_{2}, -C(O)NR'(OR'),
-C(S)NR'(OR'); -C(O)NR'(SR'), -G(S)NR'(SR'), -CH(CN)_2,
-CH[C(0)R']_2, -CH[C(S)R']_2, -CH[C(O)OR']_2, -CH[C(S)OR']_2,
-CH[C(0)SR'], and -CH[C(S)SR'],;
      each R is independently selected from the group
consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6)
alkynyl, (C_5-C_{20}) aryl, substituted (C_5-C_{20}) aryl, (C_6-C_{26})
alkaryl and substituted (C6-C26) alkaryl
      the heterocycloalkyl substituents are each independently
selected from the group consisting of -CN, -NO2, -NR'2, -OR',
-C(0)NR'_2, -C(S)NR'_2, -C(0)OR', -C(S)OR', -C(0)SR', -C(S)SR'
and trihalomethyl;
     the aryl and alkaryl substituents are \each independently
selected from the group consisting of halogen, -C(0)R';
-C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'<sub>2</sub>,
-C(S)NR', and trihalomethyl;
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each R' is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl and (C_1-C_6)

--- designates a single or double bond.

4. The pharmaceutical composition of Claim 3, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C;

alkynyl; and

Y is absent, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl;

 R_1 is absent -H, -OR, =0, -NR₂, =N-OR, -O-C(O)R, or when taken together with R_2 is 3-5 membered oxirane or 3-5 membered substituted oxirane;

R, is absent or -H;

R, is absent or -H;

 R_4 is -H, -OR, -NR₂, -CN, -C(O)OR, -C(O)NR₂ or 5-6 membered dioxoycycloalkyl;

each R_s , R_s and R_r is independently selected from the group consisting of -R', -F, -Cl or -Br;

each R is independently selected from the group consisting of -H, (C_1-C_3) alkyl, (C_1-C_3) alkenyl, (C_5-C_{10}) aryl, substituted (C_5-C_{10}) aryl, (C_6-C_{13}) alkaryl, substituted (C_6-C_{13}) alkaryl;

the oxirane substituent is -CN, $-NO_2$, $-NR'_2$, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(0)R', -C(0)OR' and trihalomethyl;

R' is -H, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl; and

--- is a single or double bond.

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A method of inhibiting mammalian cell proliferation, said method comprising the step of contacting a mammalian cell in situ with an effective amount of a compound having the structural formula:

$$(R_{5})_{n}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

$$(R_{7})_{m}$$

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

m is 0, 1, 2, 3 or 4;

each n is independently 0, 1, 2, 3, 4 or 5;

X is C;

Y is absent, (C_1-C_6) alkyl, (C_1-C_6) alkenyl or (C_1-C_6) alkynyl;

 R_1 is absent, -OR, -SR, =O, =S, =N-OR, -O-C(O)R, -S-C(O)R, -O-C(S)R, -S-C(S)R, or when taken together with R, is a 3-8 membered heterocycloalkyl or a substituted 3-8 membered heterocycloalkyl;

R₂ is absent or -H;

R, is absent or -H;

 R_4 is -H, -OR', -SR', -NR'₂, -CN, -NO₂, (C_3 - C_8) cycloalkyl, 3-8 membered heterocycloalkyl, -C(0)R', -C(5)R', -C(0)OR', -C(S)OR', -C(O)SR', -C(S)SR', $-C(O)NR'_2$ or $-C(S)NR'_2$;

each Rs, Rs and R, is independently selected from the group consisting of -halogen, -R', -OR', -SR'\ -NR'2, -ONR'2, $-SNR'_2$, $-NO_2$, -CN, -C(O)R', -C(S)R', -C(O)OR', $\frac{1}{2}C(O)SR'$, -C(S)OR', -CS(S)R', $-C(O)NR'_2$, $-C(S)NR'_2$, -C(O)NR'(OR'),

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> -C(S)NR'(OR'); -C(S)NR'(SR'), -C(S)NR'(SR'), -CH(CN)₂, -CH[C(O)R']₂, -CH[C(S)R']₂, -CH[C(O)OR']₂, -CH[C(S)OR']₂, -CH[C(O)SR']₂ and -CH[C(S)SR']₂;

> each R is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_5-C_{20}) aryl, substituted (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl and substituted (C_6-C_{26}) alkaryl;

the heterocycloalkyl substituents are each independently selected from the group consisting of -CN, -NO₂, -NR'₂, -OR', -C(0)NR'₂, -C(5)NR'₂, -C(0)OR', -C(5)OR', -C(0)SR', -C(5)SR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of halogen, -C(0)R', -C(S)R', -C(O)OR', -C(O)OR', -C(O)SR', -C(O)SR', -C(O)NR', and trihalomethyl;

each R' is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkynyl; and

--- designates a single or double bond.

7. The method of Claim 6, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C,

Y is absent, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl;

 R_1 is absent -H, -OR, =O, -NR₂, =N-OR, -O-C(O)R, or when taken together with R_2 is 3-5 membered oxirane or 3-5 membered substituted oxirane;

R₂ is absent or -H;

R, is absent or -H; .

R₄ is -H, -OR, -NR₂, -CN, -C(0)OR, -C(0)NR₂ or 5-6 membered dioxoycycloalkyl;

each R_s , R_s and R_r is independently selected from the group consisting of -R', -F, -Cl or -Br;

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each R is independently selected from c_{12} group consisting of -H, (C_1-C_3) alkyl, (C_1-C_3) alkynyl, (C_5-C_{10}) aryl, substituted (C_5-C_{10}) aryl, (C_6-C_{13}) alkaryl, substituted (C_6-C_{13}) alkaryl,

the oxirane substituent is -CN, -NO $_2$, -NR $'_2$, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(0)R', -C(0)OR' and trihalomethyl;

R' is -H, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl; and

--- is a single or double bond.

11. The method of Claim 10, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C;

Y is absent, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl;

 R_1 is absent -H, -OR, =O, -NR₂, =N-OR, -O-C(O)R, or when taken together with R_2 is 3-5 membered oxirane or 3-5 membered substituted oxirane;

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R, is absent or -H;

R, is absent or -H;

 R_{\star} is -H, -OR, -NR₂, -CN, -C(0)OR, -C(0)NR₂ or 5-6 membered dioxoycycloalkyl;

each R_5 , R_6 and R_7 is independently selected from the group consisting of -R', -F, -Cl or -Br;

each R is independently selected from the group consisting of -H, (C_1-C_3) alkyl, (C_1-C_3) alkenyl, (C_5-C_{10}) aryl, substituted (C_5-C_{10}) aryl, (C_6-C_{13}) alkaryl, substituted (C_6-C_{13}) alkaryl;

the oxirane substituent is -CN, -NO₂, -NR'₂, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(0)R', -C(0)OR' and trihalomethyl;

R' is -H, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl; and

--- is a single or double bond. --

H 4